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CONFERENCE REPORTS AND EXPERT PANEL

Recommendations for mechanical ventilation of critically ill children from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC)

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Abstract

Purpose: Much of the common practice in paediatric mechanical ventilation is based on personal experiences and what paediatric critical care practitioners have adopted from adult and neonatal experience. This presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted interventions. We aim to establish a European consensus guideline on mechanical ventilation of critically children.

Methods: The European Society for Paediatric and Neonatal Intensive Care initiated a consensus conference of international European experts in paediatric mechanical ventilation to provide recommendations using the Research and Development/University of California, Los Angeles, appropriateness method. An electronic literature search in PubMed and EMBASE was performed using a combination of medical subject heading terms and text words related to mechanical ventilation and disease-specific terms.

Results: The Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) consisted of a panel of 15 experts who developed and voted on 152 recommendations related to the following topics: (1) general recommendations, (2) monitoring, (3) targets of oxygenation and ventilation, (4) supportive measures, (5) weaning and extubation readiness, (6) normal lungs, (7) obstructive diseases, (8) restrictive diseases, (9) mixed diseases, (10) chronically ventilated

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Take-home message: Much of the common practice in paediatric mechanical ventilation is based on personal experiences and what paediatric critical care practitioners have adopted from adult and neonatal experience. This presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted interventions. The PEMVECC guidelines should help to harmonise the approach to paediatric mechanical ventilation and thereby propose a standard-of-care applicable in daily clinical practice and clinical research.

patients, (11) cardiac patients and (12) lung hypoplasia syndromes. There were 142 (93.4%) recommendations with "strong agreement". The final iteration of the recommendations had none with equipoise or disagreement.

Conclusions: These recommendations should help to harmonise the approach to paediatric mechanical ventilation and can be proposed as a standard-of-care applicable in daily clinical practice and clinical research.

Keywords: Mechanical ventilation, Physiology, Paediatrics, Lung disease

Introduction

Huge variability in size, lung maturity and the range of acute and chronic diagnoses have contributed to a lack of clinical evidence supporting the daily practice of paediatric mechanical ventilation (MV) (Fig. 1) [1, 2]. This prompted the Respiratory Failure Section of the European Society for Paediatric and Neonatal Intensive Care (ESPNIC) to convene the paediatric mechanical ventilation consensus conference (PEMVECC), aiming to harmonise the approach to paediatric MV and define a standard-of-care applicable in clinical practice and future collaborative clinical research. Specific aims were to provide recommendations regarding ventilation modalities, monitoring, targets of oxygenation and ventilation, supportive measures, and weaning and extubation readiness for patients with normal lungs, obstructive airway diseases, restrictive diseases, mixed diseases and chronically ventilated patients, cardiac patients and lung hypoplasia syndromes, and to provide directions for further research. From 138 recommendations drafted, 34 (32.7%) did not reach "strong agreement" and were redrafted (i.e. rewriting or rephrasing sometimes into two different recommendations), resulting in 52 recommendations for the second voting round. Of these, 142 (93.4%) reached "strong agreement".

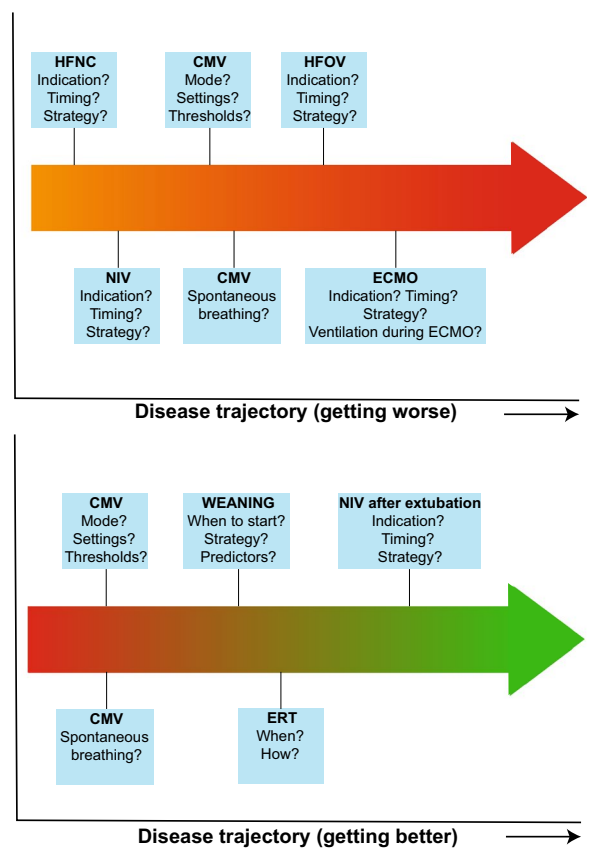

Fig. 1 Graphical simplification of the gaps in knowledge regarding paediatric mechanical ventilation as a function of disease trajectory when the patient is getting worse or is getting better

Methods

The steering committee (M.K. (chair), D.d.L., J.B., P.B. and P.R.) defined disease conditions (see ESM) and identified ten European panel members who were internationally established paediatric MV investigators with recent peer-reviewed publications (last 10 years). An electronic literature search in PubMed and EMBASE (inception to September 1, 2015) was performed using a combination of medical subject heading terms, text words related to MV and disease-specific terms. All panel members screened the references for eligibility, defined by (1) age <18 years, (2) describing non-invasive or invasive respiratory support, and (3) type of design (i.e. any type of clinical study except for case-series and reports). Publications were excluded if they described diseases exclusively linked to the perinatal period. The proposal by Chatburn (ESM, Table 2) was used for ventilator taxonomy [3, 4].

Recommendations were drafted by all panel members, and subsequently discussed at a two-day meeting in Rome, Italy (September 2015). This resulted in a final set of recommendations, subjected to electronic voting (December 2015) using the Research and Development/University of California, Los Angeles (RAND/UCLA) appropriateness method scale [5]. Recommendations were scored from 1 (complete disagreement) to 9 (complete agreement). Median score (95% confidence interval) was calculated after eliminating one lowest and highest value. Recommendations were labelled "strong agreement" (median 7–9 and no score <7), "equipoise" (median 4–6) or "disagreement" (median 1–3). Recommendations without "strong agreement" were rephrased. Revised recommendations retaining "strong agreement" after the second electronic voting (February 2016) were

labelled "weak agreement" and the percentage of agreement (number of individual scores ≥7 divided by 15) quantified the level of disagreement. As it was expected a priori that there would be very few RCTs or systematic reviews, it was decided by the steering committee to keep the consensus guideline descriptive and not use the GRADE system [6].

Non-invasive support

High-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP)

There is insufficient data to recommend on the use of HFNC in obstructive airway (strong agreement), restrictive (strong agreement) or mixed disease (strong agreement) or on the use CPAP in obstructive airway (strong agreement) or restrictive disease (93% agreement). CPAP may be considered if there are no contra-indications (strong agreement) as initial support in mixed disease (strong agreement) and mild-to-moderate cardiorespiratory failure (strong agreement). There is insufficient data to recommend on the optimal interface for CPAP (strong agreement).

Although HFNC or CPAP may reduce the work of breathing, there are no outcome data showing superiority of HFNC or CPAP over any other intervention [7–28].

Non-invasive ventilation (NIV)

NIV can be considered before resorting to intubation in obstructive airway (strong agreement), restrictive disease (93% agreement), mild-to-moderate PARDS (strong agreement) or cardiorespiratory failure (strong agreement). NIV should not delay endotracheal intubation, but no specific limits can be provided in any disease condition (strong agreement). There are no data to recommend on any method or timing of NIV (strong agreement). There are insufficient data to provide recommendations on the optimal interface for NIV. Any interface with the least leakage needs to be used (strong agreement). Dependent on local experiences and materials, full face mask, oral-nasal mask or helmet for NIV should be used (93% agreement).

Non-invasive ventilation (NIV) is increasingly being used in ARF [29–32], after cardiac surgery for congenital heart disease [33–36], status asthmaticus [37, 38], or neuromuscular patients with ARF [39–41]. Few uncontrolled studies suggested improved extubation success with NIV [42, 43]. Two RCTs comparing NIV versus oxygen supplementation on intubation prevention produced opposing results [43, 44]. In adult studies, NIV increased adverse outcomes in severe ARDS [45–52]. To avoid delayed intubation, success of NIV should be assessed already 1 h after initiation by observing heart and respiratory rate, SpO_2/FiO_2 ratio, pH, level of consciousness and presence of organ failure [44, 50, 53].

Ventilator modes

We cannot make recommendations on any mode of mechanical ventilation for children with normal lungs (strong agreement), obstructive airway (strong agreement), restrictive (strong agreement), mixed disease (strong agreement), chronically ventilated children (strong agreement), cardiac children (strong agreement) or children with lung hypoplasia (strong agreement). With restored respiratory drive, pressure support ventilation may be considered. If used, the sensitivity of the flow cycling and rise time should be set to obtain an appropriate inspiratory time (strong agreement). There are no outcome data to recommend on closed-loop ventilation (strong agreement).

There are no outcome data to recommend on any ventilatory or respiratory assist modes for children with or without lung pathology, cardiac children, or chronically ventilated children requiring escalation of support for acute exacerbations [2, 54–59]. Ventilator mode should be dictated by clinical experience and theoretical arguments, considering the pathophysiology of the disease [60, 61].

There are insufficient data to recommend on high-frequency oscillatory ventilation (HFOV) in obstructive airway (strong agreement), restrictive (strong agreement), mixed disease (strong agreement), cardiac children (strong agreement), chronically ventilated children or children with a congenital disorder who suffer from an acute exacerbation (93% agreement). HFOV may be considered if conventional ventilation fails (strong agreement), using an open lung strategy to maintain optimal lung volume. Careful use of HFOV can be considered in cardiac children who developed severe respiratory failure. Particular caution is advised in children with passive pulmonary blood flow or right ventricular dysfunction (strong agreement).

A mortality benefit of HFOV in acute hypoxaemic respiratory failure (AHRF) has not been shown [62]. Recent retrospective cohort analyses seemed to confirm adult observations of even an increased mortality with HFOV, although major methodological issues have been raised regarding these studies [63–71]. HFOV can judiciously be performed in obstructive airway disease and cardiac children, including those with a Fontan circulation [72–78].

There are insufficient data to recommend on high-frequency jet or high-frequency percussive ventilation (strong agreement) or airway pressure release ventilation (strong agreement). HFJV should not be

used in obstructive airway disease because of the risk of dynamic hyperinflation (strong agreement).

There are no outcome data supporting high—frequency jet (HFJV) or high—frequency percussive ventilation (HFPV) for any disease condition outside the operating theatre when managing children with airway disorders [79–85].

We recommend considering extra-corporeal devices (ECMO or other devices) where available in reversible diseases if conventional and/or HFOV fails. If no ECMO is available, early consultation of an ECMO centre is recommended because transporting patients who need ECMO can be hazardous (strong agreement).

All aspects of ECMO in paediatric ARF are discussed in a Statement paper [86].

Setting the ventilator

Triggering

We recommend targeted patient ventilator synchrony in any triggered (non-invasive) positive pressure ventilation (strong agreement).

The effects of patient-ventilator asynchrony or interventions such as flow cycling on outcome are unclear [87–89]. However, better patient ventilator synchrony has been shown to improve patient comfort [89–92].

Setting the I:E ratio/inspiratory time

We recommend setting the inspiratory time and respiratory rate related to respiratory system mechanics and disease trajectory. Both are closely correlated and cannot be judged as independent from each other (strong agreement). In restrictive lung disease, we recommend a higher respiratory rate to compensate for low tidal volume and maintain minute ventilation (strong agreement).

There are no outcome data to guide the choice of inspiratory time or I:E ratio. However, the time constant (i.e. compliance times resistance) of the respiratory system (π) is an important parameter in this context. At the bedside, we suggest to avoid flow end-inspiratory or expiratory flow interruption, the latter to avoid air-trapping.

Maintaining spontaneous breathing

We recommend that all children on respiratory support preferably should breathe spontaneously, with the exception of the most severely ill child with obstructive airway (strong agreement), restrictive (strong agreement) or mixed disease (strong agreement) requiring very high ventilator settings and intermittent neuromuscular blockade (strong agreement). In these children, controlled mechanical ventilation (pressure or volume) should be preferred, mandating the need for continuous sedation and/or muscle relaxants (strong agreement). Caution is advised when using sedation and relaxation in the presence of cardiac dysfunction (strong agreement).

Although there are no data to recommend on maintaining spontaneous breathing, adult data suggest that maintaining spontaneous breathing during MV allows for a more homogeneous lung aeration and reduced risk of muscular atrophy and diaphragmatic dysfunction [93–97]. In adults, 48-h use of neuromuscular blocking agents (NMBA) in early severe ARDS significantly reduced 90-day crude mortality [98]. The only paediatric uncontrolled study on NMBA showed improved oxygenation [99]. No outcome data are available.

Setting the pressures

In the absence of transpulmonary pressure measurements, we recommend limiting the plateau pressure (Plat) ≤28 cmH_2O (87% agreement) or ≤29–32 cmH_2O if the chest wall elastance is increased in restrictive lung disease (93% agreement), mixed disease (strong agreement) and children with congenital/chronic disorders (strong agreement). We recommend limiting Pplat ≤30 cmH_2O in obstructive airway disease (strong agreement).

Observational studies in (severe) lung injury identified a direct relationship between peak inspiratory pressure (PIP) and mortality [100–103]. Measuring transpulmonary pressure (Ptp) instead of airway pressure (Paw) better defines lung strain in (severe) lung injury, especially in the presence of increased chest wall elastance [104, 105]. However, there are no studies identifying upper limits for PIP, Pplat or Ptp. For severe disease, we recommend adhering to the Pediatric Acute Lung Injury Consensus Conference (PALICC) recommendations [106].

We recommend delta pressure (i.e. the difference between end inspiratory and end expiratory pressure) <10 cmH_2O if there is no lung pathology (strong agreement). There are no data to recommend any acceptable delta pressure in restrictive (strong agreement), obstructive airway (strong agreement) or mixed disease (strong agreement). For children with reduced lung volumes, the driving pressure at zero-flow (Vt/Crs) may dictate the optimal tidal volume (Vt) (strong agreement).

Driving pressure (ΔP = Vt/Crs) best stratified the risk for mortality in adults with ARDS [107]. These observations have not been replicated in children except for one study reporting an independent association between the airway pressure gradient (difference between PIP and PEEP) and mortality measured under dynamic flow conditions [103].

Setting tidal volume

There are no data to recommend optimal Vt in restrictive (strong agreement), obstructive airway (strong

agreement), mixed disease (strong agreement), in cardiac children (strong agreement), children with congenital disorders or chronic ventilation (strong agreement. We recommend targeting physiologic Vt (strong agreement) and to avoid Vt > 10 mL/kg ideal bodyweight (strong agreement). In children with lung hypoplasia syndromes, optimal Vt may be smaller than physiologic because of the lower lung volumes (strong agreement).

So far, not a single value of Vt has been associated with mortality in children, irrespective of disease severity (i.e. ALI/ARDS vs. non-ALI/ARDS) [108, 109]. Interestingly, some observational studies reported better outcomes for children who were ventilated with Vt > 5–8 ml/kg and only one identified lower mortality associated with Vt ~8 mL/kg actual bodyweight compared with ~10 mL/kg [100, 101, 110–112].

Setting PEEP

We recommend PEEP to prevent alveolar collapse. However, we cannot recommend how much PEEP should be used. Physiological data in children without lung injury suggests 3–5 cmH_2O (strong agreement). In severe disease, high PEEP may be needed (strong agreement). PEEP should always be set finding the optimal balance between haemodynamics and oxygenation. In order to improve oxygenation, PEEP titration should be attempted. There is no defined method to set best PEEP (strong agreement).

Moderate PEEP is sufficient when there is no lung pathology, but higher PEEP to restore EELV and improve respiratory system compliance (Crs) may be necessary in more severe disease and does not impair haemodynamics [1, 113–121]. There are no data comparing low versus high PEEP in (severe) lung injury. Also, it is unclear how to set PEEP and whether markers such as PaO_2 or quasi-static Crs predict best PEEP [122].

In obstructive airway or mixed disease, there are no data to recommend the level of PEEP in sedated and/or paralysed children who have sufficient expiratory times. However, assessment of intrinsic PEEP and Pplat may guide setting external PEEP in children with air trapping who are mechanically ventilated and sedated (strong agreement). A balance needs to be found between alveolar recruitment and alveolar overdistension (strong agreement).

There are no data supporting external PEEP to attenuate gas-trapping by splinting the airways open or guiding the allowable amount of external PEEP to facilitate spontaneous breathing [123–126].

We recommend using high PEEP to stabilise airways in ventilated children with trachea- and/or bronchomalacia. Careful titration of PEEP is mandated to avoid cardiovascular compromise (strong agreement).

Observational data suggested reduced respiratory efforts with PEEP or CPAP in children with upper airway collapse. If used, it should be lowly titrated to avoid hemodynamic compromise [127, 128].

Lung recruitment

There are insufficient data to recommend any lung recruitment manoeuvre in children with (strong agreement) or without (strong agreement) lung injury or in cardiac children (strong agreement).

Recruitment manoeuvres (RM) may resolve atelectasis and improve gas exchange, but there are no data showing improved outcome [129–136]. There are no outcome data to recommend on the best RM (i.e. sustained inflation or PEEP titration) [115, 137–139]. There is no indication for routine RMs after endotracheal suctioning [140].

Monitoring

Recommendations and long text on monitoring can be found in the ESM.

Targets for oxygenation and ventilation

Oxygenation

We cannot recommend a specific lower or upper limit for SpO_2 for any ventilated non-cardiac child with obstructive airway, restrictive or mixed disease (strong agreement). SpO_2 >95% at room air should be expected in children without lung injury and extra-pulmonary manifestations (strong agreement). We recommend adhering to the PALICC guidelines for PARDS (i.e. SpO_2 92–97% when PEEP <10 cmH_2O and 88–92% when PEEP ≥10) (strong agreement). We cannot recommend a specific upper or lower limit for SpO_2 for cardiac children. In children with cardiorespiratory failure, oxygen therapy should be titrated, balancing pulmonary disease against the underlying cardiac disorder, as well as in some conditions (e.g., single ventricle physiology) balancing pulmonary versus systemic blood flow (strong agreement). Increasing FiO_2 up to 1.0 in life-threatening acute pulmonary hypertension crisis may be required (strong agreement).

There are no studies identifying the optimal SpO_2 range in the presence or absence of lung injury. In healthy children breathing room air, SpO_2 >95% and PaO_2 between 80 and 100 mmHg should be expected [141, 142]. In cardiac children, children with or at risk for lung injury or children with pulmonary hypertension, target SpO_2 depends on the type and severity of laesions [143, 144]. PALICC proposed SpO_2 between 92 and 97% when PEEP <10 cmH_2O and 88–92% for PEEP ≥10 cmH_2O in non-cardiac PARDS [106]. There are no data reporting the safety and necessity of liberal or restrictive oxygen

therapy, but as a rule of thumb the lowest FiO_2 should be targeted [145–147].

Ventilation

We recommend achieving normal CO_2 levels in children with normal lungs (strong agreement). For acute (non-)pulmonary children, higher levels of CO_2 may be accepted unless specific disease conditions dictate otherwise. However, we cannot recommend any specific pH limit. We recommend permissive hypercapnia targeting a pH > 7.20 (strong agreement). In children at risk for pulmonary hypertension, we recommend to maintain normal pH (strong agreement). We recommend using pH as non-pharmacologic tool to modify pulmonary vascular resistance for specific disease conditions (strong agreement).

There are no studies identifying optimal CO_2 in the presence or absence of lung injury. Normal CO_2 levels (i.e. 35–45 mmHg) should be expected in healthy children. Increasing ventilator settings in an attempt to normalise mild hypercapnia may be detrimental [148]. There are no outcome data on the effects of permissive hypercapnia or the lowest tolerable pH [149, 150]. Normal pH and PCO_2 should be targeted in severe traumatic brain injury and pulmonary hypertension.

Weaning and extubation readiness testing

There are insufficient data to recommend on the timing of initiation (strong agreement) and approach to weaning (strong agreement) and the routine use of any extubation readiness testing that is superior to clinical judgement (strong agreement).

Assessing daily weaning readiness may reduce duration of ventilation [150–152]. There are no data supporting superiority of any approach such as protocolised weaning, closed-loop protocols, nurse-led weaning, or the usefulness of predictors for weaning success [123, 151, 153–172]. There are no data to recommend how to perform and evaluate extubation readiness testing (ERT), although some studies suggest that using a minimum pressure support overestimates extubation success [173–175].

There are insufficient data to recommend the routine use of non-invasive respiratory support after extubation for any patient category. However, early application of NIV combined with cough-assist techniques should be considered in neuromuscular diseases to prevent extubation failure (strong agreement).

There is only one small pilot study suggesting that the use of NIV may prevent reintubation in children at high-risk for extubation failure [42]. Although appealing, post-extubation NIV in combination with cough-assist techniques has not been confirmed to prevent extubation failure in neuromuscular patients yet [176–179].

Supportive measures

Humidification, suctioning, positioning and chest physiotherapy

We recommend airway humidification in ventilated children, but there are insufficient data to recommend any type of humidification (strong agreement).

There are no data showing superiority or inferiority of either active or passive humidification [180–182]. However, there is great variability amongst commercially available HMEs regarding humidification efficacy, dead space volumes and imposed work of breathing [183].

There are insufficient data to recommend on the approach to endotracheal suctioning (strong agreement), but the likelihood of derecruitment during suctioning needs to be minimised (strong agreement). The routine instillation of isotonic saline prior to endotracheal suctioning is not recommended (strong agreement).

There is no scientific basis for routine endotracheal suctioning or the approach to suctioning (open vs. closed) albeit that open suctioning may lead to more derecruitment or the instillation of isotonic saline prior to suctioning [140, 184–188].

There are insufficient data to recommend chest physiotherapy as a standard of care (strong agreement). Use of cough-assist techniques should be considered for patients with neuromuscular disease on NIV to prevent failure (strong agreement).

Chest physiotherapy for airway clearance and sputum evacuation cannot be considered standard of care [189, 190]. It is unclear whether cough-assist techniques add any value to patients with neuromuscular disease who require NIV, but their use should be considered to prevent endotracheal intubation [176, 178, 191–195].

We recommend that all children should be maintained with the head of the bed elevated to 30–45°, unless specific disease conditions dictate otherwise (strong agreement).

Endotracheal tube and patient circuit

Endotracheal high-volume low-pressure cuffed tubes can be used in all children. Meticulous attention to cuff pressure monitoring is indicated (strong agreement).

Cuffed ETTs can be safely used without increased risk for post-extubation stridor when the cuff pressure is

maintained ≤20 cmH_2O [196, 197]. Cuff pressure monitoring has to be routinely performed using cuff-specific devices [198].

Dead space apparatus should be reduced as much as possible by using appropriate patient circuits and reduction of swivels (strong agreement).

Any component that is added after the Y piece increases dead space and may have clinical relevance [199].

Double-limb circuits should be used for invasive ventilation (strong agreement), and preferentially a single-limb circuit for NIV (93% agreement).

Single-limb circuits are very sensitive to leaks [200]. Therefore, single-limb home ventilators are not suitable for invasive ventilation in the PICU [201].

Miscellaneous

We recommend avoiding routine use of hand-ventilation. If needed, pressure measurements and pressure pop-off valves should be used (strong agreement).

Manual ventilation should be avoided to prevent the delivery of inappropriate high airway pressure and/or volume [202].

Specific patient populations

Lung hypoplasia

Recommendations for children with acute restrictive, obstructive or mixed disease should also be applied to children with lung hypoplasia syndromes who suffer from acute deterioration (strong agreement).

Chronically ventilated/congenital patient

In severe or progressive underlying disease, we recommend considering whether or not invasive ventilation is beneficial for the particular child (strong agreement). For chronic neuromuscular children and other children on chronic ventilation with acute deterioration, the same recommendations as for children with normal lungs, acute restrictive, acute obstructive or mixed disease are applicable (strong agreement). Preservation of spontaneous breathing should be aimed for in these children (strong agreement).

Invasive ventilation may be life-saving, but the risk/benefit ratio should be carefully evaluated in each ventilator-dependent child who suffers from acute exacerbations or in children with life-limiting congenital disorders [203–208]. In the absence of data, we suggest that the recommendations for children with acute restrictive, obstructive or mixed disease are also applicable in this patient category.

Cardiac children

Positive pressure ventilation may reduce work of breathing and afterload in LV failure, but it may increase afterload in RV failure (strong agreement). In cardiac children with or without lung disease, the principles for any specific pathology will apply, but titration of ventilator settings should be carried out even more carefully (strong agreement). We cannot recommend on a specific level of PEEP in cardiac children with or without lung disease, irrespective of whether or not there is increased pulmonary blood flow, but sufficient PEEP should be used to maintain end-expiratory lung volume (strong agreement).

Many of the assumptions on cardiopulmonary interactions in children are mainly based on adult data [209–212]. For cardiac children, assisted rather than controlled ventilation may be preferable [57, 59]. However, in patients with passive pulmonary blood flow, spontaneous breathing on CPAP 3 5 cmH_2O reduced FRC and increased PVRI, whereas MV with PEEP 3–5 cmH_2O did not [213]. Neither CPAP nor PEEP ≤15 cmH_2O impaired venous return or cardiac output after cardiac surgery [214–217]. This means that, for cardiac children, the same principles for MV apply as for non-cardiac children [211, 218].

Reflecting on the consensus conference

Our consensus conference has clearly but also painfully emphasised that there is very little, if any, scientific evidence supporting our current approach to paediatric mechanical ventilation (Fig. 1; Tables 1, 2). Given this absence of evidence, our recommendations reflect a consensus on a specific topic that we agreed upon. To date, most of what we do is either based on personal experiences or how it works in adults. In fact, when it comes to paediatric MV "each paediatric critical care practitioner is a maven and savant and knows the only correct way to ventilate a child" (by Christopher Newth). This lack of scientific background should challenge everybody involved in paediatric mechanical ventilation to embark on local or global initiatives to fill this huge gap of knowledge. We are in desperate need of well-designed studies and must constantly remind us that "Anecdotes" are not plural for "Evidence" [219–221]. This European paediatric mechanical ventilation consensus conference is a first step towards a better and substantiated use of this life-saving technique in critically ill children (Figs. 2, 3, 4).

Table 1 Overview of published literature related to all aspects of paediatric mechanical ventilation for the disease conditions discussed in the consensus conference

Subject	Available data		Applicability to specific disease conditions
	RCT	Observational	
Non-invasive support			
Use of HFNC	None	Yes	Healthy lungs, all disease conditions
Use of CPAP	None	Yes	All disease conditions
Non-invasive ventilation	Yes ($n = 2$)	Yes	All disease conditions
Ventilator modes			
Conventional modes	None	Yes	Healthy lungs, all disease conditions
HFOV	Yes ($n = 2$)	Yes	All disease conditions
HFJV, HFPV	No	Yes	All disease conditions
Liquid ventilation	No	No	All disease conditions
ECMO	No	Yes	All disease conditions
Setting the ventilator			
Patient-ventilator synchrony	No	Yes	All disease conditions
I:E ratio/inspiratory time	No	No	All disease conditions
Maintaining spontaneous breathing	No	No	Healthy lungs, all disease conditions
Plateau pressure	No	No	Healthy lungs, all disease conditions
Delta pressure/driving pressure	No	No	Healthy lungs, all disease conditions
Tidal volume	No	Yes	Healthy lungs, all disease conditions
PEEP	No	Yes	Healthy lungs, all disease conditions, upper airway disorders
Lung recruitment	No	Yes	Healthy lungs, all disease conditions
Monitoring			
Ventilation	No	Yes	Healthy lungs, all disease conditions
Oxygenation	No	Yes	Healthy lungs, all disease conditions
Tidal volume	No	Yes	Healthy lungs, all disease conditions
Lung mechanics	No	Yes	Healthy lungs, all disease conditions
Lung ultrasound	No	Yes	All disease conditions
Targets for oxygenation and ventilation			
Oxygenation	No	No	Healthy lungs, all disease conditions
Ventilation	No	No	Healthy lungs, all disease conditions
Weaning and extubation readiness testing			
Weaning	Yes ($n = 2$)	Yes	Healthy lungs, all disease conditions
NIV after extubation	No	Yes	All disease conditions
Use of corticosteroids	Yes	Yes	Healthy lungs, all disease conditions
Supportive measures			
Humidification	No	Yes	Healthy lungs, all disease conditions
Endotracheal suctioning	No	Yes	Healthy lungs, all disease conditions
Chest physiotherapy	No	Yes	All disease conditions
Bed head elevation	No	No	Healthy lungs, all disease conditions
ETT and patient circuit	No	Yes	Healthy lungs, all disease conditions
Reducing dead space apparatus	No	Yes	Healthy lungs, all disease conditions
Heliox	No	Yes	Obstructive airway disease
Use of manual ventilation	No	No	Healthy lungs, all disease conditions

Table 2 Potential clinical implications of the recommendations from the paediatric mechanical ventilation consensus conference (PEMVECC)

Non-invasive support	
High-flow nasal cannula	No recommendation
Continuous positive airway pressure	Consider in mixed disease Consider in mild-to-moderate cardiorespiratory failure No recommendation on optimal interface
Non-invasive ventilation	Consider in mild-to-moderate disease, but not severe disease Consider in mild-to-moderate cardiorespiratory failure Should not delay intubation No recommendation on optimal interface
Invasive ventilation	
Mode	No recommendation
High-frequency oscillatory ventilation	Consider when conventional ventilation fails May be used in cardiac patients
High-frequency jet/percussive ventilation	No recommendation Do not use high-frequency jet ventilation in obstructive airway disease
Liquid ventilation	Do not use
Extra-corporeal life support	Consider in reversible disease if conventional ventilation and/or HFOV fails
Triggering	Target patient-ventilator synchrony
Inspiratory time/I:E ratio	Set inspiratory time by respiratory system mechanics and underlying disease (use time constant and observe flow-time scalar). Use higher rates in restrictive disease
Maintaining spontaneous breathing	No recommendation
Plateau pressure	Keep $\leq$28 or $\leq$29–32 cmH_2O with increased chest wall elastance, $\leq$30 cmH_2O in obstructive airway disease
Delta pressure	Keep $\leq$10 cmH_2O for healthy lungs, unknown for any disease condition
Tidal volume	Keep $\leq$10 mL/kg ideal bodyweight, maybe lower in lung hypoplasia syndromes
PEEP	5−8 cmH_2O, higher PEEP necessary dictated by underlying disease severity (also in cardiac patients) Use PEEP titration, consider lung recruitment (also in cardiac patients) Add PEEP in obstructive airway disease when there is air-trapping and to facilitate triggering Use PEEP to stent upper airways in case of malacia
Monitoring	
Ventilation	Measure PCO_2 in arterial or capillary blood samples Consider transcutaneous CO_2 monitoring Measure end-tidal CO_2 in all ventilated children
Oxygenation	Measure SpO_2 in all ventilated children Measure arterial PO_2 in moderate-to-severe disease Measure pH, lactate and central venous saturation in moderate-to-severe disease Measure central venous saturation as marker for cardiac output
Tidal volume	Measure near Y-piece of patient circuit in children <10 kg
Lung mechanics	Measure peak inspiratory pressure and/or plateau pressure, mean airway pressure, positive end-expiratory pressure. Consider measuring transpulmonary pressure, (dynamic) compliance, intrinsic PEEP Monitor pressure–time and flow-time scalar
Lung ultrasound	Consider in appropriately trained hands
Targets	
Oxygenation	$SpO_2 \geq$ 95% when breathing room air for healthy lungs No threshold for any disease condition or cardiac patients, but keep $SpO_2 \leq$97% For PARDS: SpO_2 92–97% when PEEP < 10cmH_2O and 88–92% when PEEP $\geq$10 cmH_2O
Ventilation	PCO_2 35–45 mmHg for healthy lungs Higher PCO_2 accepted for acute (non-)pulmonary patients unless specific diseases dictate otherwise Target pH >7.20 Target normal pH for patients with pulmonary hypertension
Weaning and extubation readiness	
Weaning	Start weaning as soon as possible Perform daily extubation readiness testing
Non-invasive ventilation after extubation	Consider non-invasive ventilation in neuromuscular patients
Corticosteroids	Use in patients at increased risk for post-extubation stridor

Table 2 continued

Supportive measures	
Humidification	Use humidification
Endotracheal suctioning	Do not perform routinely, only on indication. No routine instillation of isotonic saline prior to suctioning
Chest physiotherapy	Do not use routinely Consider using cough-assist devices in neuromuscular patients
Positioning	Maintain head of bed elevated 30–45°
Endotracheal tube and patient circuit	Use cuffed endotracheal tube, keep cuff pressure ≤20 cmH_2O Minimise dead space by added components Use double-limb circuits for invasive ventilation Do not use home ventilators during the acute phase in the intensive care unit
Miscellanenous	
Hand-ventilation	Avoid hand ventilation unless specific conditions dictate otherwise

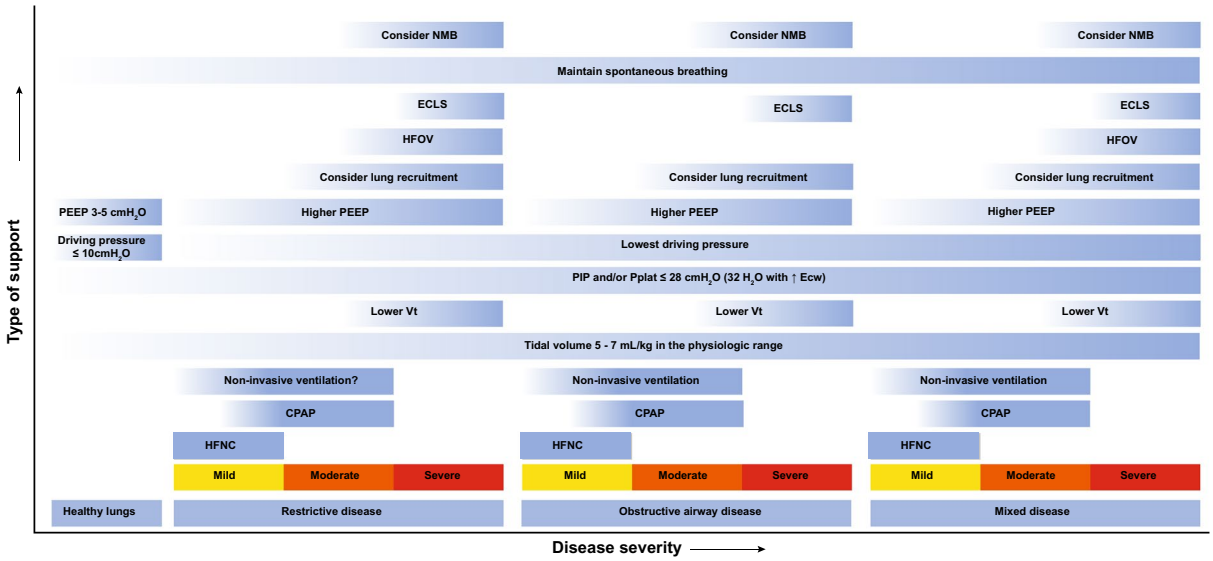

Fig. 2 Graphical simplification of the recommendations on "ventilator mode", "setting the ventilator" and "supportive measures" in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The *colour gradient* denotes increasing applicability of a specific consideration with increasing disease severity. *Absence of the colour gradient* indicates that there is no relationship with disease severity. The *question mark* associated with specific interventions highlights the uncertainties because of the lack of paediatric data. *HFNC* high flow nasal cannula, *CPAP* continuous positive airway pressure, *NIV* non-invasive ventilation, *PIP* peak inspiratory pressure, *Pplat* plateau pressure, *Vt* tidal volume, *PEEP* positive end-expiratory pressure, *HFOV* high-frequency oscillatory ventilation, *ECLS* extra-corporeal life support, *NMB* neuromuscular blockade

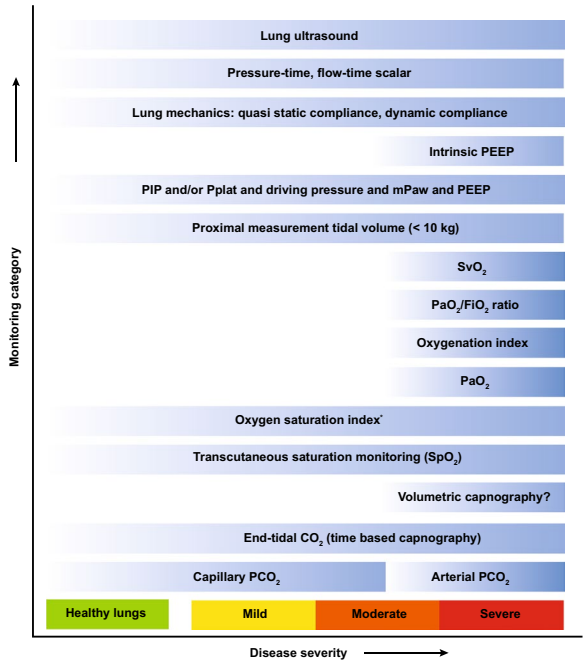

Fig. 3 Graphical simplification of the recommendations on "monitoring" in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The *colour gradient* denotes increasing applicability of a specific consideration with increasing disease severity. *Absence of the colour gradient* indicates that there is no relationship with disease severity. The *question mark* associated with specific interventions highlights the uncertainties because of the lack of paediatric data. *PIP* peak inspiratory pressure, *Pplat* plateau pressure, *Vt* tidal volume, *PEEP* positive end-expiratory pressure, *mPaw* mean airway pressure, *SvO_2* venous oxygen saturation

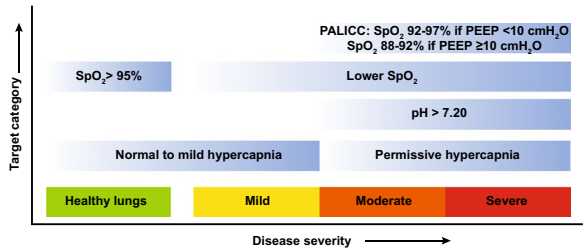

Fig. 4 Graphical simplification of the recommendations on "targets of oxygenation and ventilation" in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The *colour gradient* denotes increasing applicability of a specific consideration with increasing disease severity. *Absence of the colour gradient* indicates that there is no relationship with disease severity. The *question mark* associated with specific interventions highlights the uncertainties because of the lack of paediatric data. PALICC pediatric acute lung injury consensus conference

Electronic supplementary material

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Compliance with ethical standards

Conflicts of interest

The authors declare the following conflicts of interest: M.K. received research funding from Stichting Beatrix Kinderziekenhuis, Fonds NutsOhra, ZonMW, UMC Groningen, TerMeulen Fonds/Royal Dutch Academy of Sciences and VU university medical center and serves as a consultant for and has received lecture fees from Vyaire. His institution received research technical support from Vyaire and Applied Biosignals. P.B. received honoraria from Abbvie, a travel grant from Maquet and served on an advisory board for Masimo. F.R. received consultancy fees from Vitalaire and Philips Respironics. P.R. received travel support from, Maquet, Acutronic, Nycomed, Philips, to run international teaching courses on mechanical ventilation. His institution received funding from Maquet, SLE, Stephan (unrestricted funding for clinical research) and from the European Union's Framework Programme for Research and Innovation Horizon2020 (CRADL, Grant no. 668259). M.P. received honoraria from Air-liquide Healthcare and served as speaker for Fisher & Paykel and ResMed. His institution received disposable materials

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